

**REMARKS**

Reconsideration and allowance of the pending claims is respectfully requested. Claims 3-16, 21-22, and 28 are now pending in the instant application, claims 1 and 23-27 having been canceled without prejudice or disclaimer. Claims 3, 4, 7, 9 and 22 have been amended to correct dependencies and to more clearly recite the subject matter deemed the invention. Support for the amended claims can be found throughout the application as filed, particularly in the originally filed claims. Applicants respectfully submit that no new matter will be introduced into the application via these amendments to the claims.

Claims 23-27 were rejected under 35 U.S.C. § 112, first paragraph, for containing subject matter allegedly not enabled by the specification. Applicants have canceled these claims without prejudice or disclaimer, rendering moot this rejection.

Claims 1, 3-7, 9-12, 14-16, 21 and 22 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No.: 5,585,254 (hereinafter Maxwell '254). Claims 8, 13, 21 and 28 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Maxwell '254. The Examiner cites Maxwell '254 for its disclosure of "autonomous Parvoviral gene delivery vehicles and expression vectors". Applicants note that Maxwell '254, filed April 2, 1993 and published December 17, 1996, is a Continuation-in-part of U.S. Serial No.: 07/685,628, filed April 15, 1991, which was a Continuation-in-part of Serial No.: 07/088,086 August 21, 1987. Applicants respectfully submit that Maxwell '254 does not constitute prior art to the instant claims, which are directed to a nucleotide sequence comprising, *inter alia*, the nucleotide sequence of an

oncoselective autonomous parvovirus for the destruction or normalization of cancer cells.

Maxwell '254 did not disclose an autonomous parvovirus as gene delivery vehicles for the destruction of cancer cells until filed as a Continuation-in-part on April 2, 1993. For example, Applicants direct the Examiner's attention to page 9 of the Serial No.: 07/685,628, filed April 15, 1991, wherein viral vectors are generally described for the introduction of chimeric toxin genes into target cells. However, only retroviral vectors are described for this purpose. No alternative viral vectors are suggested for this purpose, and no direction is given as to where a skilled artisan might turn for further guidance. Maxwell '254, actually discourages the use of recombinant retrovirus vectors for gene delivery, as they are "quite labile, grow to relatively low titers (particularly recombinant retroviruses), are difficult to handle without significant infectivity loss, and exhibit a limited host range". See Maxwell '254 at column 1, lines 50-62. Thus, the pre-1993 disclosures of the parent and grandparent of Maxwell '254 do not sufficiently guide a skilled artisan toward the invention and, thus, fails to constitute prior art to the instant claims.

By contrast to the parent and grandparent applications from which Maxwell '254 claims priority, Applicants respectfully submit that the instant application and its priority documents contain specific examples showing that it is possible to use the oncoselective characteristics of autonomous parvovirus to target cancer cells with a toxic agent. In particular, Applicants submit that several examples show it is possible to introduce a cytotoxic polypeptide to a cell, a molecule that confers to the transfected cell sensitivity to a toxic agent, or a polypeptide that increases an immune response. Unlike

the retroviral vectors of the priority applications of Maxwell '254, the parvoviral constructs according to the invention can be produced in high amounts, and retain oncoselectivity against cancer cells.

Therefore, in view of the disclosures of Maxwell '254, only the specification of the Continuation-part of filed April 2, 1993 teaches the use of autonomous parvoviral vectors for delivering genes to targeted cells. Applicants note that this 1993 date is later in time than the December 10, 1992 filing date of the Belgian application from which priority is claimed. Accordingly, Maxwell '254 does not constitute prior art under Section 102 or Section 103.

In view of the above remarks and amendments, Applicants respectfully submit that the application is in condition for allowance. Notification to that effect is earnestly solicited.

Respectfully submitted,

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APPENDIX

MARK UP VERSION SHOWING CHANGES MADE

**IN THE CLAIMS:**

The claims have been amended as indicated below.

3. (Amended) The nucleotide sequence according to claim 10 [2],  
wherein the virus is chosen from the group consisting of [the] parvovirus H1,  
[the] fibrotropic parvovirus variant of [the "] Minute virus of Mice ["] (MVMP)  
and [the] parvovirus Lulli.

4. (Amended) The nucleotide sequence according to claim 10 [1],  
wherein the virus nucleotide sequence lacks nucleotide sequences encoding  
the parvovirus capsid proteins VP1 and VP2.

7. (Amended) The nucleotide sequence according to claim 1 wherein  
the effector nucleotide sequence comprises at least two coding nucleotide  
sequences, [and/or] non-coding nucleotide sequences, or combinations  
thereof, operably linked in polycistronic subunits under the control of a single  
promoter unit.

9. (Twice Amended) The nucleotide sequence according to claim 10  
[1], wherein the effector nucleotide sequence encodes at least one fusion  
polypeptide containing at least one ligand selected [chosen] from the group

consisting of the hypervariable end specific of an antibody, a cytokine [or] and a growth factor, wherein the ligand binds specifically to at least one molecule expressed at the surface of cancerous or infected cells.

22. (Amended) The recombinant vector comprising the sequence or a portion of the sequence according to claim 10 [1].

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